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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/526,348	03/16/2000	Dr. Guido Bojack	514413-3817	2532

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FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/526,348	BOJACK ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/1/03 (amdt)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

No claims have been cancelled, claims **1 and 14** have been amended, the abstract has been amended, and the disclosure has not been amended as per the amendments filed October 1, 2003. No additional Information Disclosure Statements (IDSs) have been received.

Claims **1-21** remain in the case.

Claims **1-21** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows.

A. The breadth of the claims is excessive in view of the number of specific embodiments listed in the Tables at pages 63-123 (11 examples) when compared with the total number of examples (a total of 698 separate examples are listed at pages 63-123).

B. The nature of the invention is compounds which are adenosine deaminase (ADA) inhibitors and their administration to mammalian hosts in need of treatment wherein ADA inhibition is necessary, or administration to plants as a herbicide, but without sufficient guidance concerning which mammalian disease conditions are to be treated and how such treatment should proceed.

C. The state of the prior art varies widely, but in some cases is very limited because the synthesis of several of the bicyclic heterocycles is presently unknown in the prior art.

D. The level of one of ordinary skill also varies widely because of the wide variation in the amount of prior art available in either the synthetic or medicinal areas depending on the ring system selected.

E. The level of predictability in the art also varies widely because of the lack of information concerning how to make or use several of the heterocyclic systems included within the scope of the claims.

F. The amount of direction provided by the inventor is quite limited because the number of examples provided (only 11 compounds characterized), wherein only a subset were tested for biological activity, and none of these tests for biological activity were conducted on whole mammalian hosts (all *in vitro* tests).

G. The existence of working examples is very limited with only 11 compounds prepared and characterized and only 5 tested for ADA activity using rabbit ADA.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure would be very substantial because of the lack of prior art teachings to guide the synthetic efforts where the bicyclic heterocycles are previously unknown and the almost complete absence of medicinal test data to guide experimentation concerning how best to effect ADA inhibition in a complete mammalian hosts. Examiner therefore concludes that, in the absence of considerably larger quantities of both synthetic and medicinal testing data, the instant claimed subject matter could only be practiced following expenditure of an undue amount of experimentation in both the synthetic and medicinal testing areas. In addition, the vast array of substituents, nested substituents, and inoperative embodiments like SF_5 (claim **1** at line 19, claim **2** at line 5, claim **4** at line 23, etc.; a very hydrolytically unstable substituent at best) make the task of the ordinary practitioner attempting to practice the instant invention even more difficult.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant refers to *In re Wands*. Examiner respectfully responds by noting that the MPEP specifically authorized an enhanced standard of enablement for claims wherein the subject matter involves medicinal methods of treating mammalian hosts including humans: see particularly *Ex parte Balzarini,* 21 USPQ 2d 1892 (Bd Pat App & Inter, 1992; cited in the MPEP at §2107.03(III)) wherein the first part of the decision makes clear that the mere allegation of medicinal activity without any data in support thereof is insufficiently enabling. Examiner has reviewed the disclosure and only finds specific testing data for use of specific

compounds as herbicides. Additionally, examiner finds the teaching of medicinal activity found at pages 58-62 to be only a prospective disclosure. In the absence of data in support of said medicinal teaching, and in light of the guidance provided by *Balzarini*, applicant is respectfully requested to consider specific limitation of instant claim **1** and all remaining claims to herbicidal methods of treatment only. Addition of medicinal data by amendment would be treated as a new matter situation. In conclusion, examiner fails to agree with applicant's conclusory comments concerning undue experimentation, particularly with regard to medicinal administration.

Applicant notes attachments of several abstracts which applicant argues demonstrate that the group "-SF_5" is a stable substituent. The only abstract which mentions administration to any living thing is derived from the patent publication GB **2276379**, and the abstract only refers to "control of several weeds." The remainder of the abstracts mention that stable compounds can be synthesized with this substituent, but fail to mention whether the resultant compounds are stable in blood plasma or whether when exposed to mammalian tissues undergoes chemical changes including partial or complete hydrolysis of the SF_5 moiety.

The remainder of the issues noted above are deemed to be equally serious and applicant is respectfully requested to considerably narrow the scope of the instant claims, particularly in view of applicant's reliance on functional terms like "L may be attached cyclically to the bridge G via a second direct bond or via a heteroatom selected from the group consisting of N, O and S" (see the definition of "L" in claim **1**), and other similarly functional terms which by their functionality tend to overly expand the scope of the claims while simultaneously failing to provide the necessary definiteness. And then there are the multitudes of laundry-list-Markush groups of substituents the vast majority of which are not enabled by any of the instant examples. Applicant is respectfully requested to narrow the scope of the claims to more nearly conform to the examples, a process which will require deletion of most of the Markush groups from claim **1** and similar limitation of such groups in dependent claims.

Claims **1-9, 11, 14 and 18-21** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim **1** is apparently directed to a method of treating and therefore is incomplete for failure to specify either a specific disease condition being treated by said administration or -- a host in need thereof --.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant has not responded to this grounds of rejection.

In claim **4** at line 18, the term "each of the last mentioned radicals" renders the instant claim incorrect because the first of the groups referred to is "hydrogen," a group which is not subject to substitution as required by the term "unsubstituted or substituted."

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant's argument concerning claim **1** is accepted. However, claim **4** fails to clearly define which substituents are modified by the noted term.

In claim **1** at lines 54-55 (formerly lines 62-64), the variable "L" is defined as "attached cyclically to the bridge G ... via a hetero atom selected from the group consisting of N, O and S," a term which incompletely describes what is being claimed because the particular structures being referred to are not provided, and because the heteroatom "N" has three valences, only two of which are provided with substituents.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant notes examples of what is intended, but has failed to address the clarity issue by either argument or by amendment.

In claim **1** at lines 56-58 (formerly lines 65-66), the definition of Z^1 and Z^2 is incomplete because said definition has not specified which particular acids are the source of radical substituents.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

In the disclosure at the location specified by applicant's response, the definition found does not comply with 35 U.S.C. §112, second paragraph. The definition lacks definite metes and bounds because it relies on the term "for example." Therefore, the rejection has been maintained.

In claim **1** at lines 73-74 (previously lines 69-70), the terms "aryl" and "heterocyclyl" are incompletely defined for lack of an upper size limit or a specification of the nature and location of hetero atoms. See also the terms "substituted aryl,", "heteroaryl," and "substituted heteroaryl" originally at lines 78-79 and see also dependent claims.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant has failed to address the issue with either an argument or an amendment.

In claim **1** at lines 73-74 (originally lines 83-84 and 85), the terms "heterocyclyl" and "heteroaryl" which are generic to two classes of substituents appear to be incorrectly defined as compounds.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant's argument is beside the point. For example, the term "heterocyclyl" is not a "heterocyclic ring," but is -- a substituent radical derived from a heterocyclic ring --.

In claim **8** at line 8, the term "Z is a precursor of the radical G-L" is incomplete because this functional description fails to describe what the structure of "Z" is. See also claims **9 and 11**.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant argues that functional language provide adequately defined metes and bounds without providing any reasoning or precedent. Examiner respectfully disagrees but has nothing more to add in view of applicant's very brief and conclusory comments.

Claim **8** is incomplete because the term "modifying" at line 11 implies a chemical process step but fails to completely describe the process step implied. See also claim **9** at line 8 wherein the term "cyclizing" has the same problem. See also claim **11** ("condensing" and "cyclizing").

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant appears to be arguing that because applicant has generically imagined the process and has described it with functional terms, that one of ordinary skill can guess the metes and bounds of terms like "modifying," "cyclizing," "reducing," etc. and also imagine the structures of Z and G-L, even when these substituent structures have not been specified in the claim. Examiner finds this assertion to be a ridiculous defense of what is nothing more than an example of using functional terms to "hide the ball." Applicant is again respectfully requested to provide complete claims.

Claim **19** is incomplete because the term "pharmaceutical" is generic including both compounds and their compositions but fails to define what particularly is being claimed which differs from the definition of compounds found in claim **1** (lack of proper antecedent basis). If applicant intended a pharmaceutical composition, then this claim is superfluous in view of claim **18**. In addition, said claim is improperly dependent for failure to further limit the subject matter of the claim from which it depends.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

The term "pharmaceutical" standing alone is not a recognized term of art. If applicant chooses to claim a -- pharmaceutical composition-- a format for such claims is as follows: -- A pharmaceutical composition comprising {active ingredient(s)} in combination with a pharmaceutically acceptable carrier.-- Assuming claim **18** is amended to become a -- pharmaceutical composition --, then claims **19 and 20** are improperly dependent because it

fails to specify a variation of the subject matter of claim **18** (patentable weight limited to active ingredient, carrier or relative proportions thereof) and because the limitations provided are only proper in method of treating claims.

Claim **20** is indefinite for failure to specify the treatment of any particular disease condition.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant is referred to the response to the arguments concerning the rejection of claim **19** supra.

Claim **20** recites the limitation "pharmaceutical" in apparent reference to a compound and/or a pharmaceutical composition. There is insufficient antecedent basis for this limitation in the parent claim.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant is referred to the response to the arguments concerning the rejection of claim **19** supra.

Claim **21** provides for the use of "a compound as defined in claim **1**" in a process to create a pharmaceutical composition, but, since the claim does not set forth any step(s) involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. The term at lines 4-5 of this claim ("analogously to common methods") does not overcome this grounds of rejection.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant argues that the steps being claims are "analogous to methods known in the art." Examiner still does not know, and the claim does not specify, what the steps are. The claim therefore remains incomplete.

Claims **19 and 20** are rejected under 35 U.S.C. §112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim **19** as a compound or composition claim is improperly dependent for failure to further limit the subject matter of the claim from which it depends.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant is referred to the response to the arguments concerning the rejection of claim **19** supra.

Claim **20** is improperly dependent because claim **1** fails to specify the treatment of any particular disease condition.

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant is referred to the response to the arguments concerning the rejection of claim **19** supra.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

Claims **7 and 18-20** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Duffy et al.** (PTO-892 ref. **R**).

Applicant is referred to the instant reference at page 2458, column 1, Scheme 2, structure "5a."

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant argues that there is no anticipation. Examiner respectfully disagrees, noting that the definitions of G and L are so broadly drafted that the compound noted in Duffy is included within the scope of the claimed subject matter. In particular, if G is a C-1 group, L is OR^4 ($R^4 = C_2H_5$) and G is twice substituted by OR^4 (R^4 = H, geminal dihydroxy is the hydrate of a C=O), then the group G-L is -C(=O)-OEt, and the anticipation is correct as originally alleged.

Claims **7 and 18-20** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Gewald et al.** (PTO-892 ref. **U**).

Applicant is referred to the instant reference at page 1537, the compound numbered "9."

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

The species noted above differs from that originally alleged, making this a new grounds of rejection.

Claims **18-20** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Milne et al.** (PTO-892 ref. **Y**).

Applicant is referred to page 2678 of the instant reference, column 1, the compound labeled "3."

Applicant's arguments filed October 1, 2003 have been fully considered but they are not deemed to be persuasive.

Examiner agrees that claim **7** excludes the cited subject matter of Milne et al., but does not agree that the same conclusion applies to the remainder of the originally alleged claims (**18-20**) which claims, because of the peculiar way they are presented, may be read to be directed to compounds including the compounds noted in the cited reference.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
04/16/2004

/L. E. Crane, Ph.D., Esq.
Patent Examiner
Technology Center 1600